REMARKS

In view of the preceding amendments and the comments which follow, amendment and reconsideration of the Official Action of September 22, 2003 is respectfully requested by Applicant.

Amendments to claims

Claims 19, 21, 24, 25, and 26-45 have been cancelled without prejudice. Claims 26-45 are drawn to a non-elected invention.

Claim 18 has been amended to limit the recitation of organic compounds or salts thereof having a pKa value between 1.5 and 6.0 to citric acid or a citrate salt.

Claim 18 has been amended to remove the recitation that the solution is characterized by the absence of glucose-6-phosphate dehydrogenase. Claim 18 now recites that the solution is characterized by having a pH between about 2.0 and 4.0. Antecedent basis for this teaching is found in the specification in the sentence bridging pages 4 and 5. No new matter has been added, and an additional search should not be required.

Claim 20 has been amended to depend from claim 18.

Claim 54 is new. Claim 54 recites the same limitations as recited in currently amended claim 18, with the exception that the solution of claim 54 is characterized by remaining qualitatively unchanged following storage at about 2° to 8°C for 15 months. Antecedent basis for this recitation is found in the specification on page 6, lines 16-18. No new matter is recited, and an additional search should not be required.

Claims 18, 20, 22, 23, and 54 are currently pending for examination.

Rejections under 35 USC §112, first paragraph

In Paragraph 2 of the instant action, claims 18-25 have been rejected under 35 USC §112, first paragraph, as failing to comply with the written description requirement. The examiner argues that the phrase "the solution characterized by the absence of glucose-6-phosphate dehydrogenase" recited in claim 18 is regarded as new matter because neither the specification nor claims teaches or discloses a solution that specifically excludes the dehydrotgenase. Moreover, the disclosure fails to describe that the absence of glucose-6-phosphate dehydrogenase is essential to the composition of the invention. As such the new limitation is new matter that was not originally described in the specification or claims as filed.

Accordingly, Applicant has amended claim 18 by removing the phrase "the solution characterized by the absence of glucose-6-phosphate dehydrogenase". Claims 20, 22, and 23 which depend from claim 18 are thus similarly amended.

The rejection has now been avoided, and the examiner's reconsideration of the rejection of claims 18, 20, 22, and 23 under 35 USC §112, first paragraph, is respectfully requested.

In Paragraph 3 of the instant action, claims 18-25 have been rejected under 35 USC §112, first paragraph, because the specification, while being enabling for a solution comprising (a) NAD or NADP, (b) citrate/citric acid, and (c) nitrogen compounds of a specific formula, does not reasonably provide enablement for the composition comprising any organic compound with a pKa value of 1.5-6.0. The examiner argues that the specification exemplifies a functional reagent wherein citrate is included in the composition. However, the specification fails to set forth a representative number of other organic compounds with a pKa of 1.5-6.0 that would enable one skilled in the art to make or use the composition of the invention. Since a wide array of organic compounds with a variety of functions and structures have a pKa of 1.5-6.0, it would be nearly impossible

for one skilled in the art to know which organic compound would be appropriate to the invention. Moreover, the specification fails to enable one skilled in the art how to make and use the composition of the invention with any organic compound with a pKa of 1.5-6.0.

Applicant argues that a person skilled in the art to which the present invention belongs would readily and without experimentation be able to identify other compounds meeting the limitations set forth on page 4, lines 13-18, namely, organic compounds or salts derived therefrom that have a pKa value between about 1.5 and 6.0 and especially organic acids which have a complexing action and a buffering action in the pH range of 1.0 to 7.0 such as citric acid and water-soluble salts derived therefrom.

The examiner's reconsideration of this rejection of claims claims 18, 20, 22, and 23 under 35 USC §112, first paragraph, is respectfully requested.

Rejection under 35 USC §102 (b)

In Paragraph 5 of the instant action, claims 18, 19, 22, and 24 have been rejected under 35 USC §102 (b) as being anticipated by Aoyama et al., U.S. Patent No. 5,783,382 (hereinafter "Aoyama 2"). The Examiner argues that Aoyama 2 teaches compositions comprising diagnostic agents and disoxidants (abstract, claims) wherein the preferred composition comprises a coenzyme, disoxidant, and buffer (column 1, lines 54-57, and column 2, lines 61-68). Specifically, the coenzyme may be NAD or NADP, the disoxidant may be hydroxylamines, and the buffer may be citrate and borate buffers (column 5, line 46-52. It is the examiner's position that, although Aoyama 2 does not specifically disclose a composition comprising the claimed components, one skilled in the art is able to "at once envisage" the specific combination within the generic composition. Therefore, the reference anticipates the claimed subject matter.

The Examiner's arguments pertaining to the exclusion of glucose-6-phosphate dehydrogenase are now moot since that claim limitation has been deleted from Applicant's claims.

In rebuttal, Applicant respectfully points out that the disoxidant of Aoyama 2 does not comprise part of the reagent composition but is physically separated from the reagent composition. See for example column 6, lines 37-50, describing specific examples. In one example, the disoxidant is covered with a "separating container" which is then placed into a "closed container" along with a liquid diagnostic reagent. In an alternative version, the reagent composition is stored in a "separating container" which is then stored, along with the disoxidant, in a "closed container". In another variation, both the diagnostic reagent and the disoxidant are covered with different "separating containers" followed by sealing in a "closed container". Thus, Aoyama does not teach a composition comprising diagnostic agents and disoxidants as the examiner has argued.

Claim 18 recites an aqueous solution comprising an NAD or NADP coenzyme, one or more compounds selected from the group consisting of organic compounds or salts thereof having a pKa value between 1.5 and 6.0, and a nitrogen compound of a specified formula, the solution having a pH between about 2.0 and 4.0. Aoyama 2 does not anticipate such a solution. The reagent composition taught by Aoyama 2 in Example 5 comprises a solution containing NADP, a nitrogen compound (carboxymethoxylamine HCl), and a pH of 6.6. Further in Example 5, Aoyama 2 teaches that the reagent composition stored as is in a polyvinyl chloride container is not stable, but when the polyvinyl chloride container and a disoxidant are stored in a sealed polyethylene bag, stability of the stored reagent is improved.

In light of the present amendments and the above remarks, the examiner's reconsideration of the rejection of claims 18 and 22 under 35 USC §102 (b) is respectfully requested.

Rejection under 35 USC §103 (a)

In paragraph 7 of the instant action, claims 18-25 have been rejected under 35 USC §103 (a) as being unpatentable over Aoyama 2. The examiner argues that Aoyama 2 teaches stabilized compositions comprising diagnostic agents and disoxidants (abstract, claims) wherein the preferred composition comprises a coenzyme, disoxidant, and buffer (column 1, lines 54-57, and column 2, lines 61-68). Specifically, the coenzyme may be NAD or NADP, the disoxidant may be hydroxylamines, and the buffer may be citrate and borate buffers (column 5, line 46-52). It is the examiner's position that, although Aoyama 2 does not specifically disclose a composition comprising the claimed components, one skilled in the art would have been able to "at once envisage" the specific combination within the generic composition. Moreover, at the time of the claimed invention, it would have been obvious to one of ordinary skill in the art to combine the claimed ingredients with a reasonable expectation for successfully obtaining a stabile diagnostic composition.

The examiner's arguments pertaining to the exclusion of glucose-6-phosphate dehydrogenase are now moot since that claim limitation has been deleted from Applicant's claims.

The examiner admits that Aoyama 2 does not teach the specific concentrations of each component, or the pH of the compositions. However, the examiner argues that at the time of the claimed invention, it would have been well within the purview of one of ordinary skill in the art to optimize such variables as a matter of routine experimentation. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by routine practice to optimize the amounts of ingredients in the compositions of Aoyama with a reasonable expectation for successfully obtaining a stabile diagnostic composition.

By way of the present amendment, claim 18 and claims 20, 22, and 23 which depend therefrom, have been amended to recite that the aqueous solution of the invention is characterized by having a pH between 2.0 and 4.0. This distinguishes the claimed invention from that of Aoyama 2, who teaches a pH of 6.6 for the reagent composition (example 5). One skilled in the art would not be motivated to experimentally try for a lower pH, especially a pH between about 2.0 and 4.0, since such low pH's are known to render enzymes inactive, and Aoyama 2's composition contains two enzymes, hexokinase or glucokinase and glucose-6-phosphate dehydrogenase. If the skilled artisan did, however, attempt to make the composition of Aoyama 2 using a pH between about 2.0 and 4.0, then Aoyama 2's composition would no longer be useful for its intended purpose. Thus, Applicant argues that Aoyama 2 not only doesn't anticipate or suggest Applicant's invention, Aoyama 2 actually teaches away from Applicant's invention.

Thus, Applicant argues that the Examiner has failed to make a *prima facie* case of obviousness, and reconsideration of the rejection of claims 18, 20, 22, and 23 is respectfully requested.

With regard to newly added claim 54, Applicant point out that Aoyama 2 again does not teach or suggest a stabilized composition characterized by remaining qualitatively unchanged following storage at 2° to 8°C for 15 months. Indeed, Aoyama 2 admits the instability of his composition (example 5) at column 9, lines 9-17. Aoyama 2 teaches that the composition is so unstable as to require improvement of stability by storage inside another container into which a disoxidant has been placed.

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Applicant submits that his application is now in condition for allowance, and favorable reconsideration of his application in light of the above amendments and remarks is respectfully requested. Allowance of claims 18, 20, 22, and 23 at an early date is earnestly solicited.

The Examiner is hereby authorized to charge any fees associated with this Amendment to Deposit Account No. 02-2958. A duplicate copy of this sheet is enclosed.

Respectfully submitted,

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